

THE BRITISH JOURNAL OF DERMATOLOGY

APRIL 1957

FLUORESCENCE MICROSCOPY AND THE "ACANTHOLYTIC CELL".

A. JARRETT, M.B., M.R.C.P. (Edin.)

Dermatological Research Assistant, University College Hospital Medical School, London.

CIVATTE (1943) was the first to claim that one could make an absolute histological differentiation between pemphigus vulgaris and other bullous diseases such as dermatitis herpetiformis and erythema multiforme. He described the acantholytic cell and considered it to be pathognomonic of the pemphigus group. Tzanck (1948) reported his cytodagnostic method and, on the same pathological basis as Civatte, supported the latter's claim of a distinctive cell in pemphigus.

These findings were confirmed by Lever (1951, 1953) who suggested the term "benign pemphigus vulgaris" (pemphigoid) for the condition which he believes to be the monomorphic type of dermatitis herpetiformis, having large sub-epidermal blisters without acantholysis. This disease is said to have a much better prognosis than pemphigus vulgaris except in elderly patients. In the present paper the term dermatitis herpetiformis (D.H.) is used to include both this monomorphic eruption and the polymorphic variety described by Duhring. These are grouped together for the purposes of this investigation because in both conditions there are subepidermal blisters without acantholysis, and not because they are necessarily considered to be manifestations of the same essential disorder.

The main criteria for the histological separation of pemphigus from D. H. are the situation of the bulla and the presence or absence of acantholytic cells—epidermal cells that have lost their intercellular bridges and have become detached from their neighbours. They are found in pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, Darier's disease and the benign

familial pemphigus of Hailey and Hailey. The site of the blister in these conditions is intra-epidermal, as distinct from the sub-epidermal bulla of D.H. This view has gained wide acceptance and others have written in support of these findings (Rook and Whimster, 1949, 1950; Winer and Lipschultz, 1952; Director, 1952; Lever, 1953).

A few, however, have not been so willing to accept differentiation of the bullous diseases on histological findings alone. Michelson (1952) stated that he did not consider that pemphigus could be diagnosed histologically, although some useful information may be gained by this method. Zoon and Mali (1950) pointed out that the cytodiagnostic method of Tzanck is a difficult procedure for accurate interpretation. Percival and Hannay (1949) made a careful study of bullous diseases and did not find these criteria helpful, but later they conceded that the blister of pemphigus vulgaris is intra-epidermal. Hyman (1954) did not think that the histology of a blister enabled a definite distinction to be made between pemphigus and D.H. He placed clinical evaluation above histology as a method of diagnosis in bullous diseases. Goldsmith and Hellier (1954) gave a warning of the dangers of using a single histological finding as an absolute diagnostic standard.

Dermatologists have seen cases clinically indistinguishable from pemphigus vulgaris which have terminated fatally but had subepidermal blisters and no acantholysis (so-called pemphigoid). Other cases have been observed with both types of bullae. These apparent inconsistencies together with the fact that acantholytic cells are seen in Darier's disease and benign familial pemphigus, which are not fatal conditions, make the prognostic significance of the acantholytic cell suspect.

In view of these facts, it was thought that another method of study of these diseases might be of value. Histological sections from skin affected by bullous diseases were treated with a series of fluorochromes and examined with ultra-violet rays filtered through Wood's glass. The methods used for processing and "fluorochroming" the biopsies have been described by Jarrett *et al.*, (1956).

INVESTIGATION.

A fluorescence microscopy apparatus as described by Jarrett *et al.* (1956) was employed. Material from five cases of histologically typical dermatitis herpetiformis (including pemphigoid) with subepidermal blisters and no acantholysis, and five cases of histologically typical pemphigus vulgaris, all showing acantholysis, were studied. Sections were stained with haematoxylin and eosin and with a series of fluorochromes, including acridine orange, thioflavine T, thioflavine S, rhodamine 3 G.O., and primulin. Combinations of thioflavine S and T, and of rhodamine 3 G.O. and thioflavine S were used. The most useful fluorochromes for the present investigation were found to be

primulin, acridine orange, double staining with thioflavine S and T, and double staining with rhodamine 3 G.O. and thioflavine S.

When sections of pemphigus vulgaris blisters were examined by means of these fluorochromes, acantholytic cells became clearly distinct from the other epidermal cells. With primulin they fluoresced a brilliant light blue with a central dark area, the nucleus not being fluorescent with this fluorochrome.

Acridine orange gave an entirely different picture. The acantholytic cell showed a brilliant green cytoplasm with a fluorescent red nucleus. In some, however, the green cytoplasm became intermingled with yellow and orange and the nucleus became less fluorescent. In others the nucleus lost its red colour altogether and there remained only a dark central area; these cells are older and the nucleus has either died or been ejected.

With a combination of thioflavine S and thioflavine T, some acantholytic cells took on a mauve fluorescence and contrasted markedly with normal epidermal cells. The nuclei of the acantholytic cells were either pale yellow or non-fluorescent. This suggested that the nucleus was degenerating, because normal epidermal cell nuclei gave a very strong yellow fluorescence.

In addition, a combination of rhodamine 3 G.O. and thioflavine S was employed. With these fluorochromes some acantholytic cells appeared flesh coloured and were easily distinguished from the normal epidermal cells which were blue.

The five cases of dermatitis herpetiformis were also examined with the same fluorochromes, and in all these cells having the same fluorescence as those of the pemphigus blister were found. Haematoxylin and eosin sections of these D.H. cases were then carefully scrutinized under ordinary illumination, and in among the infiltrates of the blisters weakly-staining eosinophilic material was found. These eosinophilic bodies were oval or round in shape, and in some of them there appeared to be a central hole (Fig. 3). They were much more easily seen with phase-contrast microscopy (Fig. 5).

Because eosin is a fluorochrome, these sections were remounted in a non-fluorescent medium (Gurr's "DePeX"). Canada balsam gives a blue fluorescence and is therefore unsuitable. These preparations were then observed under filtered ultra-violet rays; the eosinophilic bodies then took on a golden-yellow fluorescence with a central dark zone (Figs. 3 and 4). To confirm that these were acantholytic cells, haematoxylin and eosin sections of the pemphigus series were remounted in DePeX and examined with ultra-violet rays. When a typical acantholytic cell of pemphigus is seen under this illumination it fluoresces in the same manner as do the eosinophilic bodies present in the subepidermal blisters of dermatitis herpetiformis (Figs. 1 and 2). With ordinary illumination, weakly-staining eosinophilic bodies were seen in addition to the typical acantholytic cells.

With haematoxylin and eosin staining, *only* eosinophilic material is fluor-

escent, and because of this the basophilic nuclei appear as dark, non fluorescent, areas. With this stain it is therefore impossible to ascertain whether or not nuclei are still present in the acantholytic cells. Primulin

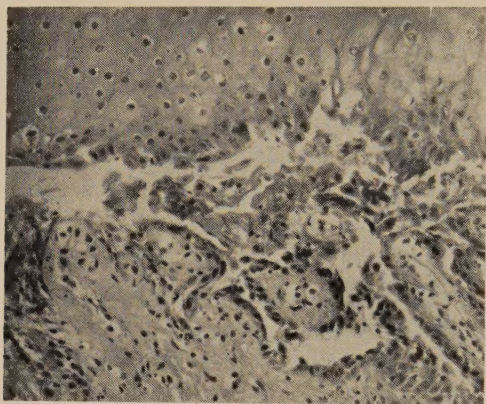


FIG. 1.—*Pemphigus vulgaris*. Typical acantholytic cells (stage 2) can be seen in the intra-epidermal cleft. H. & E. Ordinary illumination.

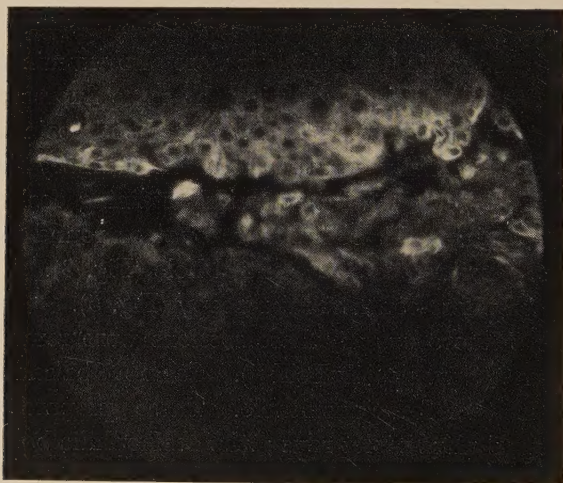


FIG. 2.—The same lesion and exactly the same field as Fig. 1 when seen by ultra-violet light. The fluorescence of the acantholytic cells is clearly shown. In addition, the epidermal cells bordering the split are fluorescing; these are early acantholytic cells (stage 1). Normal epidermal cells are non-fluorescent with this stain, and these are in the upper layers of the epidermis. H. & E. Ultra-violet illumination.

also does not cause the nuclei to fluoresce and consequently has the same limitations.

Acridine orange, and a combination of thioflavine S and thioflavine T, are

both excellent nuclear fluorochromes, and therefore the state of the nuclei can be readily determined. By this means it is possible to construct the

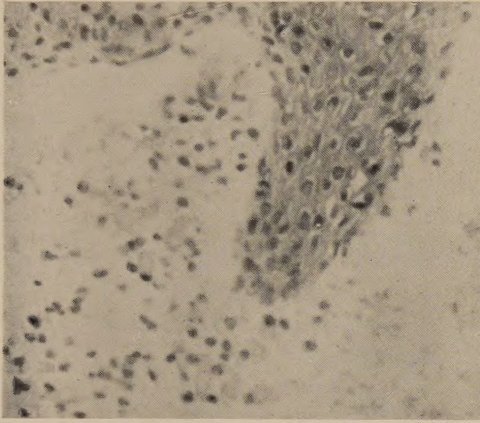


FIG. 3.—*Dermatitis herpetiformis*. A large subepidermal blister; a few acantholytic cells (stage 4) are only just visible as faintly staining eosinophilic bodies. H. & E. Ordinary illumination.

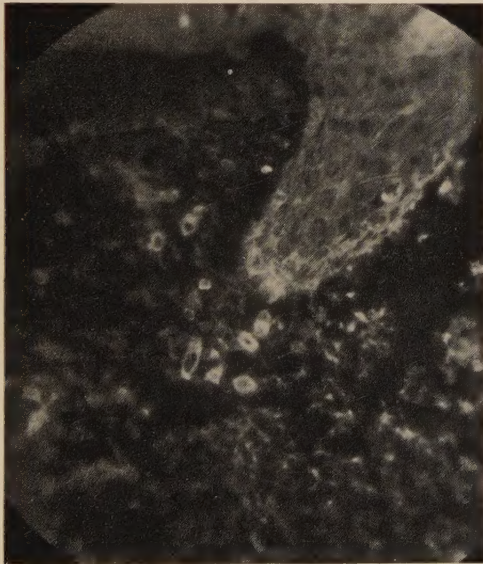


FIG. 4.—The same lesion and same field as Fig. 3, as seen with ultra-violet rays. These late acantholytic cells are fluorescing strongly, and are conspicuous. The central dark areas are holes from which the nuclei have disappeared. H. & E. Ultra-violet illumination.

sequence of events occurring in acantholysis. This is shown in Table I; the progression from normal epidermal cells to the weakly eosinophilic bodies of pemphigus and D.H. blisters is described. A study of these changes indicates

TABLE I.

Stage 0

Normal epidermal cells with intercellular bridges and basophilic cytoplasm.

Stage 1

Early acantholysis. Groups of cells become rounded and some lose their prickles. There is a slight peripheral eosinophilia of the cytoplasm, and the nuclei are more basophilic than normal.

Present in pemphigus group, Darier's disease, and in very early D. H. blisters.

Stage 2

Typical acantholytic cells. Increasing cytoplasmic eosinophilia, nuclei large, swollen, and strongly basophilic.

The "typical" acantholytic cell. Present in pemphigus group, Darier's disease, and in very early D. H. blisters. (Figs. 1 and 6-11.) The higher intrabullous tension in D. H. lesions causes a rapid progression of acantholytic cells to stage 4 and therefore these earlier stages are uncommon in older D. H. bullae.

Stage 3

Further increase of the cytoplasmic eosinophilia. The nuclei are weakly basophilic, and some cells become distorted.

Not generally recognized as an acantholytic cell. Present in blisters of pemphigus group and in some D. H. blisters.

Stage 4

Complete loss of nuclei either by death or extrusion. All the cytoplasm is eosinophilic.

Only just visible in haematoxylin and eosin sections when examined in ordinary light. Clearly visible with ultra-violet rays, and also with other suitable fluorochromes (Fig. 3, 4, and 5). Present in *all* older pemphigus blisters and in *all* older D. H. blisters.

Note.—Although the nuclear basophilism *increases* in stages 1 and 2 when examined in haematoxylin and eosin sections, suitable fluorochromes show a progressive *loss* of nuclear fluorescence from stage 0 to stage 4, indicative of a gradual nuclear degeneration.

that there is a progressive loss of nuclear fluorescence concurrent with a process of cytoplasmic keratinization. Eventually only a keratinized cell without a nucleus remains (stage 4).

This would indicate that the same process occurs in both these conditions. The only difference is that in D.H. the stages are passed through much more rapidly, and the majority of cells are in the later stages by the time biopsies are taken. They are consequently not recognized as acantholytic cells. These differences probably result from the greater intravesicular pressure in dermatitis herpetiformis; this will be discussed in more detail later.

Other disorders.

Sections from two cases of Darier's disease were treated with haematoxylin and eosin, primulin, and acridine orange. Acantholytic cells were found in both. These acantholytic cells showed the characteristic fluorescence with

acridine orange and primulin, but all the cells were in stages 1 and 2. Also, because in some areas the cells were separated from each other by only a short distance, they gave a "crazy paving" appearance to the affected epidermis. In addition, the fluorescence with eosin was weaker than with the acantholytic cells of either D.H. or pemphigus, indicating that the process of cytoplasmic keratinization had not progressed.

Artificial acantholysis produced by trypsin was very similar to that seen in Darier's disease. The same "crazy paving" pattern was present and the nuclei fluoresced well with acridine orange. As in Darier's disease, these cells fluoresced weakly with eosin.

Sections from cases of erythema multiforme and epidermolysis bullosa were also examined with the same fluorochromes. No acantholytic cells were found in the cases of erythema multiforme. In one case of epidermolysis bullosa showing relatively slight epidermal damage, a few malformed late acantholytic cells were seen in the roof of the blister. In the other cases of this disease no cells were found to give the characteristic fluorescence of the acantholytic cell. These cells were therefore not found in bullous lesions which showed severe damage to the epidermis.

DISCUSSION AND CONCLUSIONS.

The finding of acantholytic cells in cases of D.H. and pemphigus vulgaris does not imply that these two conditions are the same disease. (The classical picture of D.H. as described by Duhring is quite different from pemphigus vulgaris, both in its clinical appearance and its course.) It does mean, however, that acantholysis cannot be used as an absolute criterion to distinguish pemphigus from D.H. or from pemphigoid. Moreover, it throws doubt on the view that acantholysis represents a process of development of the intra-epidermal blister of pemphigus that is fundamentally different from that of a subepidermal lesion. This is important clinically, since some dermatologists are hesitant to use steroids when the blister is subepidermal and no acantholytic cells are found. These drugs should not be withheld on histological findings, but should be given if the bullous disease is serious or progressive.

In a subepidermal bleb, it is probable that the greater intrabullous pressure is the reason that the acantholytic cell is not seen by routine examination. Compression of the epidermal cells causes more rapid degenerative changes, and therefore a quicker progression through the stages of the acantholytic cell (Table I). These changes cause the cells to stain weakly with eosin when examined by visible light and they are consequently not seen or, if seen, are no longer recognized as epidermal cells. This point is well illustrated by one of the *intraepidermal bullae*. The patient had clinical pemphigus vulgaris but the blisters were tense. The histology showed an intra-epidermal blister but no acantholytic cells were seen when examined by ordinary illumination. Five

hundred serial sections were cut of this blister ; all showed an intra-epidermal bulla and in a few sections occasional acantholytic cells were found. When eosin and haematoxylin sections were examined by ultra-violet rays, numerous

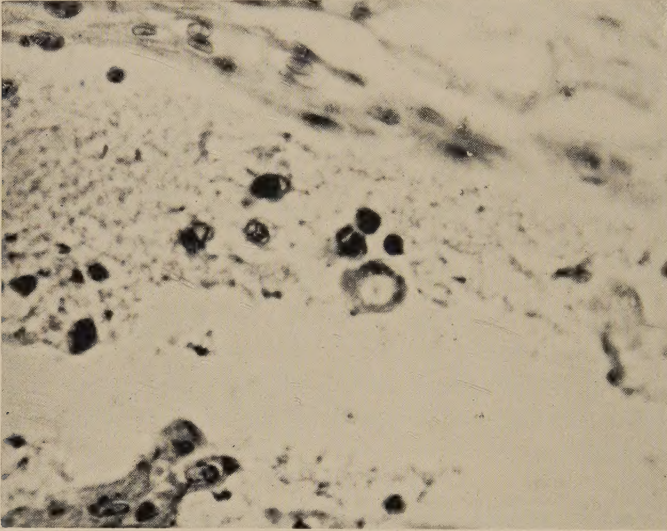


FIG. 5.—*Dermatitis herpetiformis*. Acantholytic cell stage 4. Phase-contrast microscopy shows these cells more clearly ; the central hole is obvious. H. & E. Phase-contrast $\times 680$.

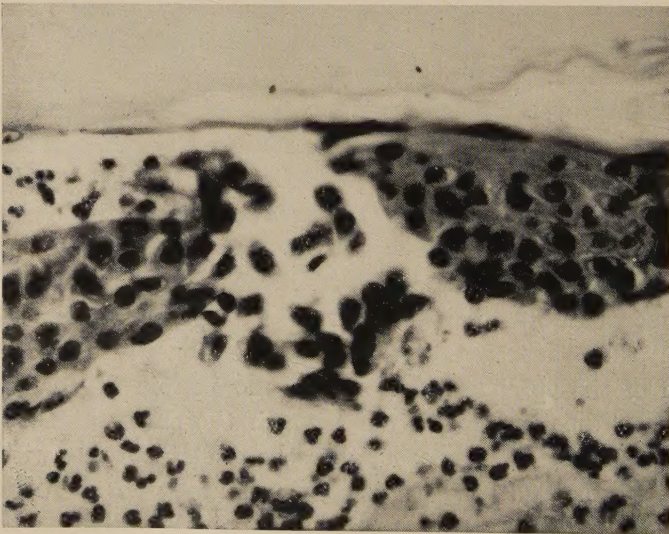


FIG. 6.—*Dermatitis herpetiformis*. Subepidermal lesion from Case 1. Typical acantholytic cells, stage 2, in the roof of the blister. There is gross disruption of the epidermal cells and almost certainly this blister would have ruptured spontaneously and not have developed into a typical tense, subepidermal bulla. H. & E. Ordinary illumination.

cells giving the characteristic fluorescence of the late acantholytic cell (stage 4) were readily seen. Thus even in an intra-epidermal blister, if the pressure is high enough, degenerative changes may be sufficiently advanced to prevent the recognition of acantholysis by routine methods.

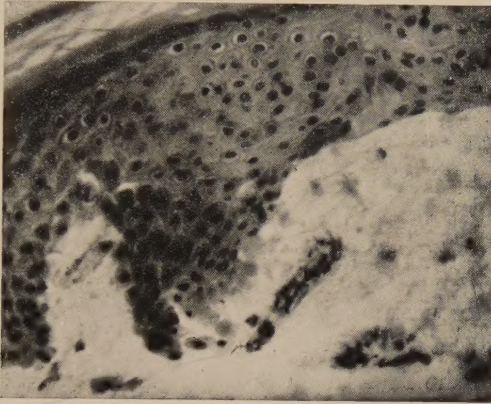


FIG. 7.—*Dermatitis herpetiformis*. Subepidermal blister from Case 2 showing acantholytic cells in stage 1. Those lining the lumen of the bulla, in the centre of the picture, have progressed to stages 3 and 4. H. & E. Ordinary illumination.

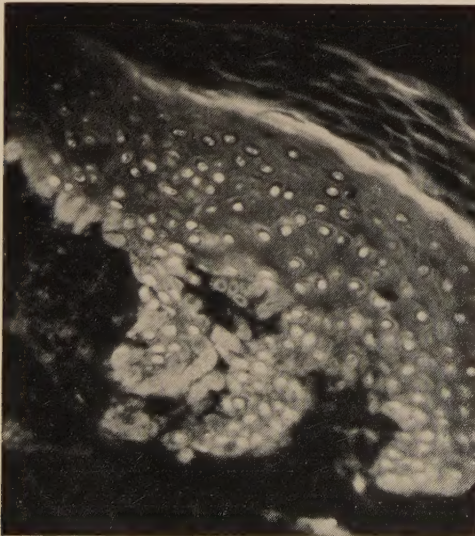


FIG. 8.—Subepidermal blister from Case 2. Acantholytic cells can be seen in all stages. In some the nuclei are brilliantly fluorescent (stages 1 and 2), in some the nuclei are dimly fluorescent (stage 3) and others have completely lost their nuclear fluorescence (stage 4). Acridine orange, ultra-violet light.

The lack of degenerative changes in the typical acantholytic cell (stage 2) has already been pointed out by Director (1952). The low pressure of the flaccid intra-epidermal blister of pemphigus vulgaris allows the individual epidermal cells to remain relatively healthy and consequently their staining reaction is little altered. When only clefts are produced, degenerative changes are minimal, and the most perfect examples of acantholytic cells are seen in Darier's disease; in this condition the process ceases at stage 2 and no cells in stages 3 or 4 can be detected.

In pemphigus vulgaris, in addition to the acantholytic cells, one can find the same weakly-staining eosinophilic bodies (stage 4) as are present in D.H. It is because of this, that often, on examination of a haematoxylin and eosin section by ultra-violet rays, many more acantholytic cells are seen than with visible light.

The examination of the acantholytic cell by various fluorochromes revealed that the colour fluorescence with any given fluorochrome approached the colour given with that fluorochrome by normal epidermal keratin. This would indicate that the fundamental change in the acantholytic cell is cytoplasmic keratinization, and it appears that the keratin produced is normal keratin (abnormal keratins often give abnormal fluorescent colours). It is important to point out that, although the colour fluorescence is that of normal keratin, this is not the normal process of keratinization. Acantholytic cells are not seen in the upper layers of a normal epidermis that is producing keratin.

In brief, the acantholytic cell appears to be an epidermal cell that is viable at the time of its separation; it then, possibly as a protective mechanism against its changed environment, undergoes a process of cytoplasmic keratinization. The nucleus becomes more and more degenerate, finally dies, and may later be extruded. It follows that grossly damaged epidermal cells can *never* become acantholytic. This is supported by the fact that these cells were never found in erythema multiforme and in only one case of epidermolysis bullosa. (This exception showed relatively slight epidermal damage.)

The histology of early lesions of dermatitis herpetiformis.

Because it was thought that the high intrabullous tension of D.H. was responsible for the scarcity of acantholytic cells in stages 1 and 2 in this condition, *very early lesions* were biopsied before any degree of intrabullous tension had time to develop. Four cases were studied in this manner and, in all, typical acantholytic cells were found in routine haematoxylin and eosin sections.

A brief history of these four cases and their response to treatment is given; the histological findings with routine staining are shown in Figs. 6-11.

Case 1. A man aged 50 years.

Itchy eruption since the age of 18. Had never been clear for more than two weeks. There were numerous papules and excoriations on the buttocks, legs and arms.

A blister was found only after a period of close observation. He was controlled by dapsone, 100 mg. daily, and was followed as an out-patient for eight months. The histology of the blister is shown in Fig. 6.

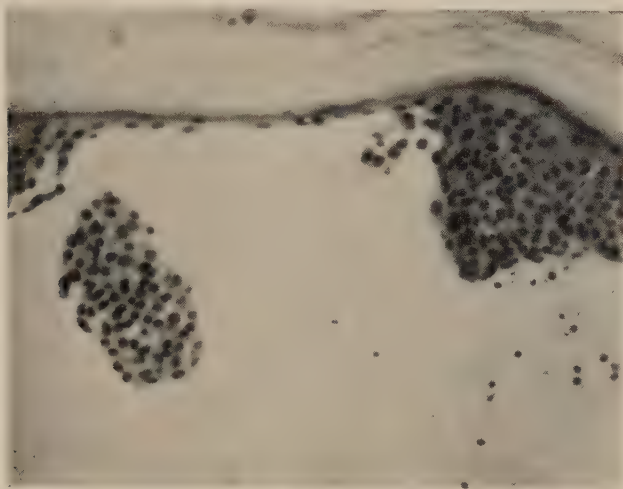


FIG. 9.—*Subepidermal blister from Case 3.* Acantholytic cells (stage 1) free within the blister and a few typical acantholytic cells (stage 2) just under the epidermis. H. & E. Ordinary illumination.

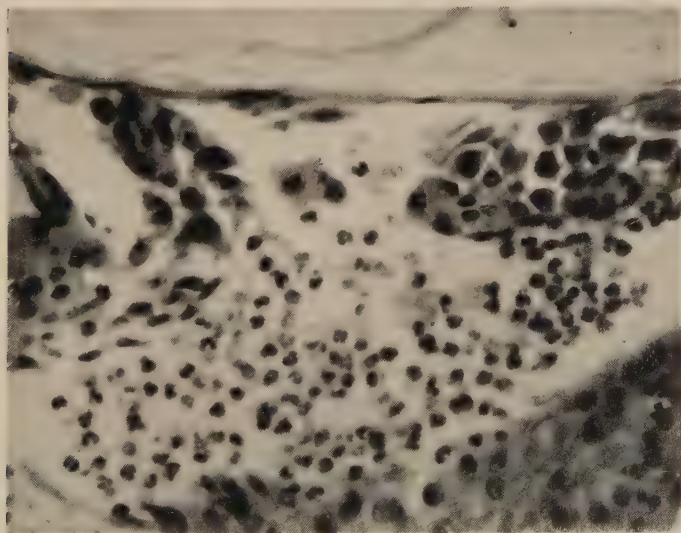


FIG. 10.—*Intra-epidermal lesion from Case 4.* Showing acantholytic cells within the cleft. H. & E. Ordinary illumination.

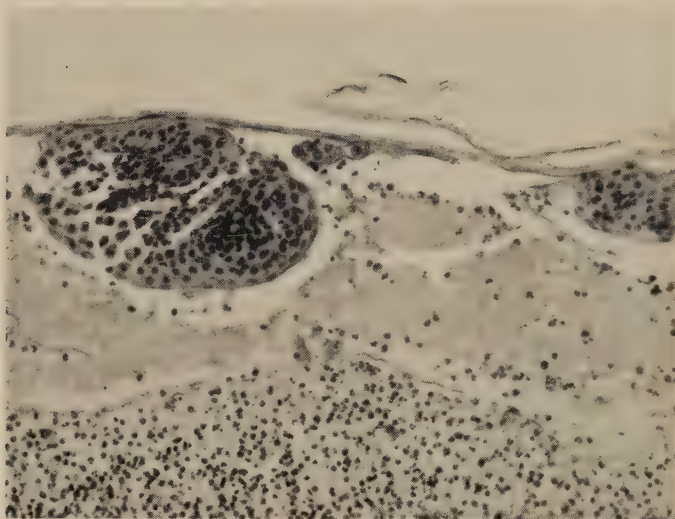


FIG. 11.—*Subepidermal blister from Case 4. Showing a group of acantholytic cells in stages 1 and 2. H. & E. Ordinary illumination.*

Case 2. A man aged 64 years.

Attacks of generalized vesicular eruption for 25 years. There were papules and excoriations on the arms, chest, and abdomen; intact vesicles were present on the face and neck. The patient suffered from intense irritation. After 50 mg. of dapsone all the lesions disappeared within 24 hours, and he was satisfactorily controlled with this dose (Figs. 7 and 8).

Case 3. A woman aged 55 years.

Onset in July, 1955, with itching eruption on elbows, buttocks, and waist. Papules and vesicles were present on the affected sites. She was dramatically relieved by dapsone 50 mg. twice daily. After six months' treatment she developed agranulocytosis but recovered with cortisone. She had subsequent partial relief with arsenic and prednisone (Fig. 9).

Case 4. A man aged 27 years.

History of two years' itchy eruption on trunk. Treated in India for allergic dermatitis. There were numerous excoriations on the trunk, and on careful examination numbers of minute vesicles were seen. He was controlled with 100 mg. of dapsone daily; there was partial relief with 50 mg. daily. He wrote from Burma seven months later stating he was remaining well on 100 mg. of dapsone daily (Figs. 10 and 11).

The histological findings in these four cases support the conclusions drawn from a study of the previous ten cases. They show that acantholysis occurs in D.H., but this is often missed because biopsies are usually taken after a high intrabullous pressure has developed. It is also worthy of note that acantholytic cells in stages 3 and 4 were not numerous in these early blisters.

SUMMARY.

Blisters from five cases of pemphigus vulgaris showing intra-epidermal lesions and acantholysis have been examined by routine methods and by fluorescence microscopy. Acantholytic cells were found to give a characteristic fluorescence which enabled them to be differentiated from normal epidermal cells.

Five cases of dermatitis herpetiformis with subepidermal blisters were similarly examined. Routine haematoxylin and eosin sections showed no typical acantholytic cells but there were numerous weakly-staining eosinophilic bodies within the blister; these have been shown to be acantholytic cells in a late stage.

The stages in the development of the acantholytic cell are described, and reasons given why the later stages have not been previously recognized.

Acantholysis was also found in Darier's disease, and in normal skin treated with trypsin. No evidence of this process was seen in cases of erythema multiforme.

Thus acantholytic cells have been demonstrated in both intra- and sub-epidermal blisters. Acantholysis itself appears to be a cytoplasmic keratinization occurring in a cell that is viable at the time of its separation. This change does not occur in bullous lesions when there is gross damage to the epidermal cells.

In four later cases of dermatitis herpetiformis, acantholytic cells have been demonstrated in routine sections examined by visible light. The biopsies were taken of very early lesions before a high intrabullous tension had time to develop.

I should like to express my gratitude to Dr. W. N. Goldsmith for his help and encouragement with this investigation. I also thank Mr. A. Bligh, photographer to University College Hospital Medical School, for his help with the production of the photofluoromicrographs, and Mrs. J. A. Hardy for the processing of the tissue.

REFERENCES.

- CIVATTE, A. (1943) *Ann. Derm. Syph., Paris*, **8**, sér. **3**, 1.
 DIRECTOR, W. (1952) *Arch. Derm. Syph., Chicago*, **65**, 155.
 GOLDSMITH, W. N. and HELLIER, F. F. (1954) *Recent Advances in Dermatology*. 2nd ed. London: J. & A. Churchill Ltd., p. 393.
 HYMAN, A. B. (1954) *Arch. Derm. Syph., Chicago*, **70**, 336.
 JARRETT, A., BLIGH, A. and HARDY, J. A. (1956) *Brit. J. Derm.*, **68**, 111.
 LEVER, W. F. (1951) *Arch. Derm. Syph., Chicago*, **64**, 727.
 ——— (1953) *Medicine, Baltimore*, **32**, 1.
 MICHELSON, H. E. (1952) *Arch. Derm. Syph., Chicago*, **65**, 422.
 PERCIVAL, G. H. and HANNAY, P. W. (1949) *Brit. J. Derm.*, **61**, 41.
 ROOK, A. J. and WHIMSTER, I. W. (1949) *Ibid.*, **61**, 223.
 ——— (1950) *Ibid.*, **62**, 443.
 TZANCK, A. (1948) *Ann. Derm. Syph., Paris*, **8**, sér. **8**, 205.
 WINER, L. H. and LIPSCHULTZ, C. E. (1952) *Arch. Derm. Syph., Chicago*, **65**, 270.
 ZOON, J. J. and MALI, J. W. H. (1950) *Dermatologica, Basel*, **101**, 145.

PYODERMA GANGRENOSUM : THE HISTOLOGY OF THE PRIMARY LESION.*

G. H. PERCIVAL.

Edinburgh University.

APART from varicose or hypostatic ulcers and so-called tropical ulcers, progressive widespread primary cutaneous ulceration is rarely seen. It is usually associated with some visceral disorder and from this standpoint cases can be divided broadly into two groups :

(i) Chronic infectious or synergistic cutaneous gangrene described by Meleney, which is associated with empyema or other visceral sepsis and develops as a post-operative complication. (ii) Chronic phagedenic ulceration, which occurs in association with ulcerative colitis. The term pyoderma gangrenosum covers both groups, but to avoid ambiguity in this paper it will be limited to the second.

In both groups there is a background of debility. Various organisms have been isolated from the ulcers and the cutaneous lesions do not respond to local antiseptic treatment or to systemic chemotherapy and antibiotics. There is no conclusive evidence that the cutaneous lesions in the two groups represent the same process. For the present, they may be regarded as distinct from one another since Meleney's ulcer mostly develops in direct anatomical continuity with a focus of visceral sepsis, whereas pyoderma gangrenosum develops at a distance from the associated visceral disorder.

The incidence of pyoderma gangrenosum as a complication of ulcerative colitis was estimated by Barga (1929) to be about 0.8%, and since 1930 a number of case reports have appeared in dermatological literature ; these have been summarised by Russell (1950) and by Clarke (1955). In the published records, the appearance of the ulcers is described, a variety of pyogenic organisms are reported to have been isolated from them, and histological examination of the edge of the ulcers revealed features common to all forms of infected non-malignant cutaneous ulceration. In a small number of cases, the primary lesion was noted as a vesicle or pustule. In one, a resemblance to the lesion of varicella was remarked on. In four cases these primary lesions were sterile, in contrast to the varied flora isolated from the actual ulcers. So far, there does not appear to be any reported histological description of the primary lesions, and the following is a record of the histological findings in a case observed recently.

* Based on a paper read at the Annual Meeting of the British Association of Dermatology in July 1956.

CASE REPORT.

The patient was a man aged 24 who had suffered from recurrent attacks of ulcerative colitis for four years. During this time no skin lesions had occurred. In December, 1954, the colitis relapsed and after three weeks a sparse eruption of purulent bullae appeared on the lower part of the trunk and thighs. Some of these lesions rapidly developed into ulcers (Fig. 1). The patient was admitted to hospital, seriously ill.

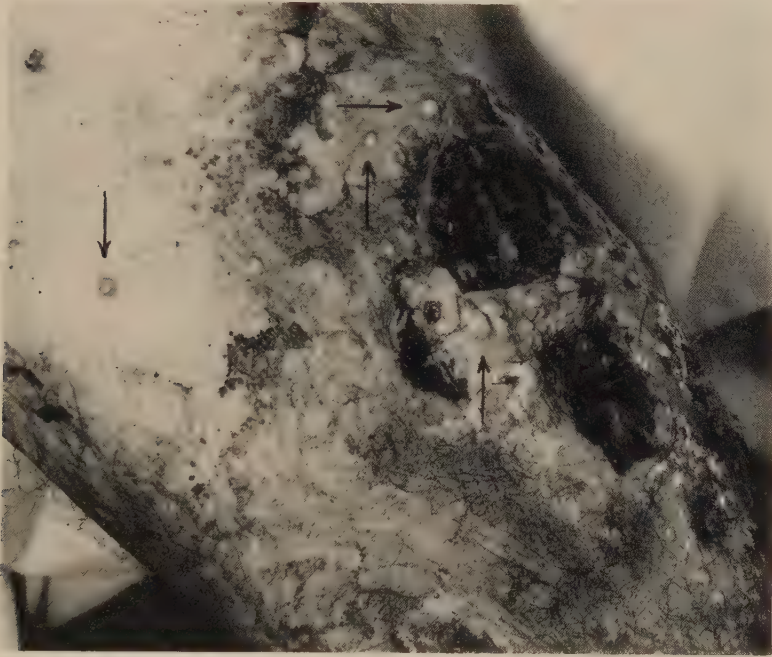


FIG. 1.—The eruption on the thigh on admission to hospital. Interspersed between the ulcers are a number of small bullae.

Cultures from unruptured purulent bullae were sterile and no organisms were found in smears. Cultures from the ulcers yielded *Staphylococcus aureus* and a scanty growth of *Esch. coli*. Blood culture was sterile. The leucocyte count was 9000 per cu. mm. when ulceration began. For a day or two after admission *S. aureus* was cultured from the stool but later it disappeared.

Treatment with cortisone was started four days after admission and a few days later the patient's general condition improved. The bowel symptoms became less severe, bullae ceased to appear, and the existing skin ulcers stopped spreading and commenced to heal. After a month this improvement was striking and several cutaneous ulcers had healed completely. ACTH was then given and the dosage of cortisone was reduced. Following this modification in treatment, improvement seemed more rapid. Four weeks later the patient was discharged; the skin had healed completely and the bowel symptoms were reduced to two motions daily. He remained well for five months, when there was a recurrence of the colitis. This was controlled by ACTH. No skin lesions accompanied the recurrence. For the past year the patient has remained well.

HISTOLOGY.

A purulent bulla, similar to those which subsequently developed into ulcers and to those whose contents were found to be sterile, was removed for histological examination by serial section. This shows that the bulla is situated in the epidermis and its cavity is packed with cells. In sections from the centre of the lesion, the roof of this cavity is formed by the stratum corneum and the major portion of the floor is composed of epidermis of varied thickness (Fig. 2).

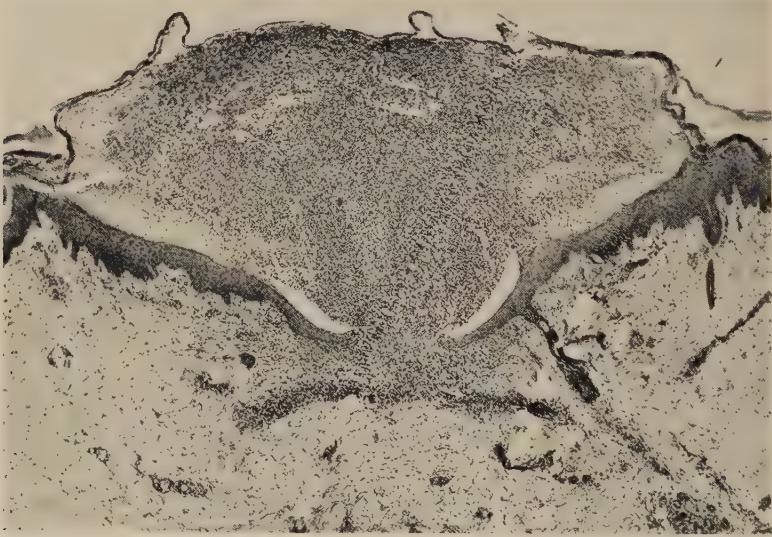


FIG. 2.—A section through the centre of the lesion. $\times 35$.

In the middle of the floor the epidermis is absent and here the floor is formed by the upper surface of the dermis. The lateral parts of the floor consist of all the epidermal layers including the stratum corneum, whereas the epidermis forming the portions adjacent to the break is reduced to a layer several cells thick. This incomplete epidermal floor might be the result of epithelial regrowth on the dermal base of a subepidermal cavity. But a comparison of the epidermal cells adjacent to the central break in the present case with those at the tip of the regrowing epithelium on the base of a subepidermal bulla suggests that the floor has not been formed in this way. The centrally-placed epidermal cells in the lesion of pyoderma gangrenosum are degenerate (Fig. 3) whereas those at the advancing edge of an epidermal regrowth are healthy in appearance (Fig. 4).

The cavity bounded by this epidermal and dermal wall is packed with lymphocytes, leucocytes and epidermal cells (Fig. 5). Lymphocytes and leucocytes are present in large numbers in the epidermal cavity, but in the papillary

layer of the dermis the reaction is restricted to a limited perivascular infiltrate confined to the area beneath the break in the epidermal floor. Obviously the leucocytic infiltration is in response to a primary epidermal crisis and is not at that moment concerned with a disease process in the dermis. This scanty

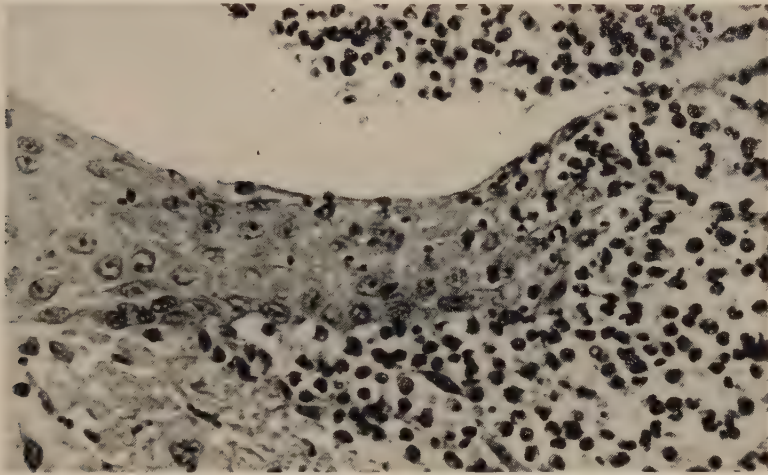


FIG. 3.—Pyoderma gangrenosum: The central portion of the epidermal floor of the cavity adjacent to the area where the floor is formed by dermis only. The epidermal cells are degenerate, and the tip of the epidermal tongue has been lifted off the surface of the dermis.

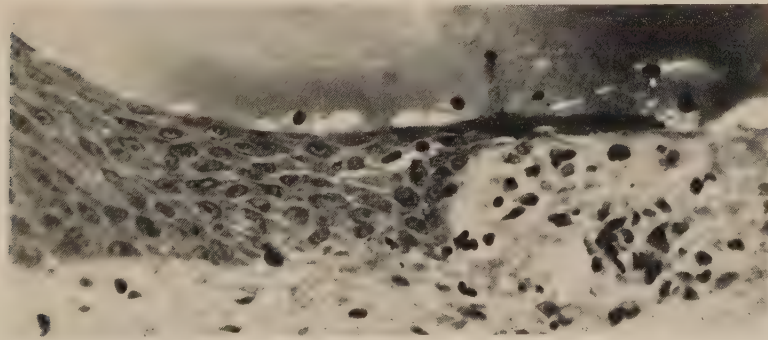


FIG. 4.—Dermatitis herpetiformis: The advancing edge of the epidermal regrowth over the dermal floor of the bulla. The epidermal cells are normal.

dermal infiltrate is much less than that seen in even quite small staphylococcal pustules. The sections of the pyoderma gangrenosum lesion include one hair follicle, but there is no evidence that it is involved in the formation of the bulla.

The epidermal cells in the cavity occur in clumps or as isolated cells and all show varied appearances of degeneration (Fig. 5). Some are small with pyknotic nuclei, resembling pemphigus cells, some are swollen and others have lost all cell structure and occur as amorphous eosinophilic masses. These degenerated epidermal cells are to be found in all parts of the cavity, from underneath its roof to its floor. These facts, together with the degenerated state of the epidermal cells adjoining the centre of the floor, and the entire absence of epidermis at the central break, suggest that a massive degenerative process has occurred extending from the basal layer to the stratum corneum. Lateral

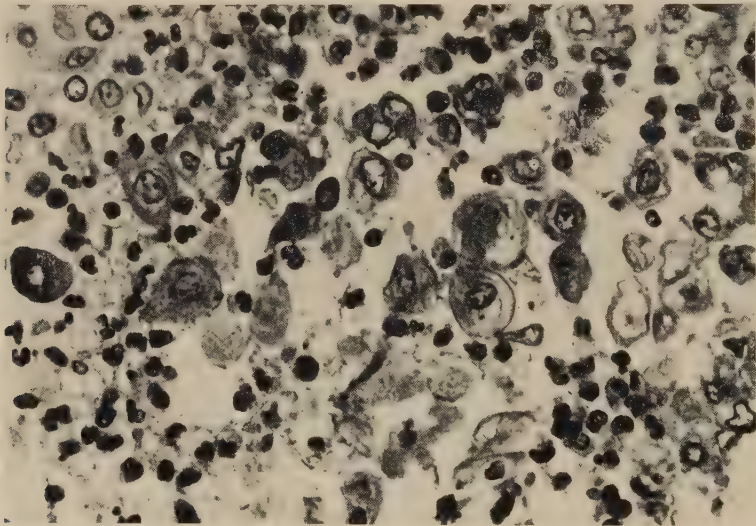


FIG. 5.—Swollen and hydropic degenerated epidermal cells in the intra-epidermal cavity.
× 440.

fissuring of the adjacent epidermis below the stratum corneum could follow this process, with the production of a bulla.

It is possible to predict from the architecture of the bulla in the middle of the lesion that sections obtained from its periphery, or indeed from the greater portion of the lesion, will show it to be entirely intra-epidermal. This is found to be so and in a great many sections the roof is formed by the stratum corneum and the entire floor by cornified epidermis. The cavity thus appears to be completely bounded by stratum corneum. The presence of degenerated epithelial cells above the stratum corneum of the bulla floor indicates that the intracorneal location of the lesion is not due to primary splitting within the original stratum corneum of the area, but to regeneration of stratum corneum on the epidermal floor of the cavity (Fig. 6). A similar appearance may be seen in the healing subcorneal bulla of pemphigus foliaceus and a completely

cornified epidermis of regrowth may be found in the floor of the subepidermal bulla of dermatitis herpetiformis. In the former disease, although degenerated cells are found in the bulla, the floor of the cavity is never formed by the dermis and in dermatitis herpetiformis the roof is formed by the entire thickness of the epidermis. In neither disease do the contents of the bullae consist of such a mass of varied types of cell.

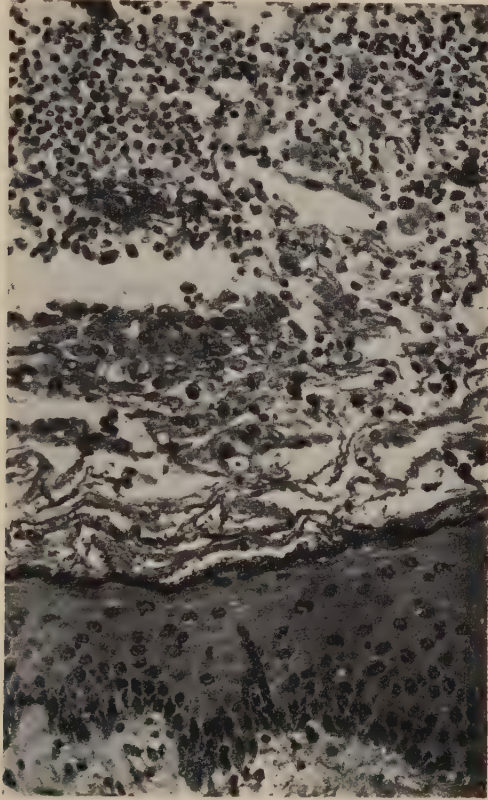


FIG. 6.—Degenerated epidermal cells lying above cornified epidermis at the periphery of the cavity. $\times 192$.

The lesion of pustular bacterid bears a close histological resemblance to the periphery of the bulla in this case, and the cellular contents of the bullae of the two diseases are similar. As far as is known, however, the cavity in pustular bacterid always has an unbroken epidermal floor.

COMMENT.

The histological findings described above suggest that the primary skin lesion in this case of pyoderma gangrenosum has developed from the action of some

factor with a specific effect on the epidermis. Investigations by Boddington and Truelove (1956) on the state of the intestinal mucosa in various active phases of ulcerative colitis have revealed the constant presence of abnormal epithelial cells, which resemble in some respects the balloon cells of herpes zoster. The authors point out that these epithelial changes may well be primary events in the intestinal disease and not the result of associated inflammation.

These observations on the state of the intestinal mucosa and the primary skin lesion in ulcerative colitis seem to indicate that primary epithelial damage may be common to both. In the case of the skin lesion just described, there seems to be no doubt that the epithelium is the tissue primarily affected. The sterility of the lesions and the histological appearance of the epidermal cells suggest that the epithelial disintegration results from the action of a chemical substance or a virus. The lack of response to antibacterial remedies by either affected tissue supports this view. Where the skin is concerned, bacterial invasion appears to be a later development. It might therefore be inferred that in both organs the lesions are produced by the same factor acting selectively on similar tissue components. If this should be so, it raises the question whether the cause first attacks the intestinal epithelium, establishes itself there and in some cases later attacks the skin, or whether it has its origin in some other focus and attacks the intestinal mucosa and the skin independently. The fact that skin ulceration has been reported to precede intestinal symptoms lends some support to the latter conjecture.

REFERENCES.

- BARGEN, J. A. (1929) *Ann. intern. Med.*, **3**, 335.
BODDINGTON, M. M. and TRUELOVE, S. C. (1956) *Brit. med. J.*, **i**, 1318.
CLARKE, D. M. (1955) *Aust. J. Derm.*, **3**, 19.
RUSSELL, B. (1950) *Brit. J. Derm. Syph.*, **62**, 114.

SOME FURTHER OBSERVATIONS ON ANGIOKERATOMA CORPORIS DIFFUSUM.

M. RUITER, M.D.

Groningen, The Netherlands.

In 1939, three brothers showing the picture of this cutaneous affection, which at that time had been practically forgotten, were sent to me for observation. These patients at the same time exhibited a number of signs and symptoms pointing to involvement of the internal organs, substantially the same in all three cases. These findings were published (Ruiter and Pompen, 1939) and the possibility was suggested of a relation between the skin changes and the accompanying internal disorder. This opinion seemed to be supported by a study of the cases known up to that time, which had been described only in the dermatological literature. The clinical picture and the differential diagnosis from other forms of angiokeratoma have been discussed elsewhere (Ruiter, 1953) and a comprehensive review given of the subject. A number of findings have come to light since 1939, and will be summarized in so far as they concern the present communication.

As a rule, angiokeratoma corporis diffusum appears before puberty and, so far, has been exclusively in males. The cutaneous lesions consist of very small lesions, only slightly, or not at all, hyperkeratotic as opposed to the angiokeratoma of Mibelli. They are more or less disseminated over the body and consist of pinhead-sized or slightly larger spots or slightly elevated papules which do not disappear on diascopic pressure. Their colour varies from purple to dark blue-red, becoming leaden-hued to black later. Histologically, the skin shows a considerable dilatation of the capillaries supplying the papillae, resulting in lacunar spaces filled with blood. The deeper blood vessels show dilatation and aneurysm formation.

The internal symptoms, which were studied for the first time in the three patients mentioned above, include vasomotor disturbances with pain and spasms in the hands, feet and thighs; persistent disturbances of sweating; swelling notably in the lower legs, cardiac enlargement and urinary abnormalities. For a long time the cause of these symptoms remained obscure in my patients, until in 1945 one of them died and an autopsy could be performed. The essential results of the pathological investigation, performed with the co-operation of Dr. H. J. G. Wyers, pathologist at the Hague, consisted in thickening of the media of the blood vessels as the result of accumulation of hyaline material between the muscle fibres and, above all, hypertrophy and

pronounced vacuolisation of the cytoplasm of the smooth muscle cells themselves. Similar enlargement and paranuclear vacuolisation were seen in the cardiac muscle fibres. The existence of a storage disease was suggested, assuming that the vacuolisation was caused by storage in the muscle cells of a substance which was not demonstrable by the staining methods used (Ruiter, 1946; Ruiter *et al.*, 1947; Pompen *et al.*, 1947).

Four years later, Scriba (1951) performed an autopsy on a similar patient in whom abnormalities were observed which, for the greater part, correspond to those described in my patients. An accumulation of lipid-like substances was demonstrated in the cardiac muscle fibres and in the smooth muscle cells of the blood vessels. These substances were also present in the ganglion cells of the brain and of the peripheral nervous system. They were also found in foam cells which were observed in the lymph glands and in the spleen. From the heart of this patient a diaminophosphatide was isolated by the biochemist Kühnau which resembled sphingomyelin in some respects but differed from it in solubility.

Since the publications discussed above, some further cases have been published. In addition to the skin affection, signs and symptoms have been described in these papers which, in the main, correspond to those found in my patients. Also foam cells and vacuolated macrophages were found in a patient recently studied by Fessas *et al.* (1955) in the urinary sediment and in bone marrow respectively. Pittelkow *et al.* (1955) mention the occurrence of necrosis of the femoral capital epiphysis in their case. The vacuolation of smooth muscle bundles which had been demonstrated by me and my co-workers, was observed in the media of cutaneous blood vessels by Fessas *et al.* and by Price (1955) and in the arrectores pilorum muscles by Pittelkow *et al.*

Apart from my histopathological investigations of the skin which will be discussed further in the present article and which have been published elsewhere (Ruiter, 1954) lipid accumulation, as seen in the autopsy material in Scriba's case, has not yet been confirmed. The death of the second of the three brothers who were the subject of my first paper provided an opportunity for an autopsy in another case.

CASE REPORT.

A man aged 47, a barber by profession, (Ruiter and Pompen (1939) Case 2). The patient showed the typical picture of angiokeratoma corporis diffusum. The skin affection had existed as long as he could remember. He often had very warm hands; sweat secretion was diminished and he had difficulty in adjusting himself to temperature changes. On the feet and lower legs there was widespread oedema for which he had worn elastic stockings for many years.

The family history contained no special features.

On examination.—The blood pressure was 160/100. Skiagram revealed marked enlargement of the left ventricle.

The urine showed constant low-grade proteinuria; the sediment contained very few white and red cells and occasional hyaline and granular casts.

E.S.R. was 9 mm./1 hour. Serum proteins normal.

Progress.—In 1946, he had a tram accident in which one of his toes was severely injured. The wound healed badly and the foot was amputated. In 1952 he was in hospital with a moderate degree of uraemia. In 1954 he was admitted to hospital in a very serious condition and with symptoms of grave gastro-enteritis and died after a couple of days. In view of subsequent findings it is noteworthy that, for many years, he had suffered from chronic gastro-intestinal complaints.

The following is mainly a report on an investigation into the occurrence of lipid storage in the internal organs of this patient. From previous skin biopsies of this patient (Ruiter, 1954), I knew that the lipoids concerned were difficult to demonstrate by staining methods.

Investigation into birefringent substances was carried out by means of frozen sections fixed in 5% formalin.

Staining methods were applied to paraffin sections. Before embedding in paraffin the formalin-fixed material remained for a week in a 3% potassium bichromate solution, which was renewed every three days (postchromation). For staining, Sudan black and scarlet red (fresh solution) were used. With this technique satisfactory staining of the lipoids could be obtained. With scarlet red the lipid was stained an orange-red colour, while Sudan black produced deep staining of the lipid granules. All sections were mounted in glycerin jelly.

As a routine, both polarized light and staining (Sudan black and haematoxylin-scarlet red) were used for demonstration of lipoids in the organs of the present case.

The findings can be summarized as follows :

Heart (H. & E.) : Vacuolisation of the muscle fibres ; the vacuoles were optically empty, apart from occasional lipofuscine. With polarized light the muscle bundles showed a birefringent substance. In paraffin sections (haematoxylin-scarlet red or Sudan black) this substance was stained orange-red or black.

Aorta : Vacuolisation of the muscle bundles of the media (H. & E.). In polarized light abundant doubly refractile substances were present in the smooth muscle fibres, which showed vacuolisation. With scarlet-red and Sudan black respectively the vacuoles appeared to be filled with aggregates of small granules which stained orange-red or black (Fig. 1).

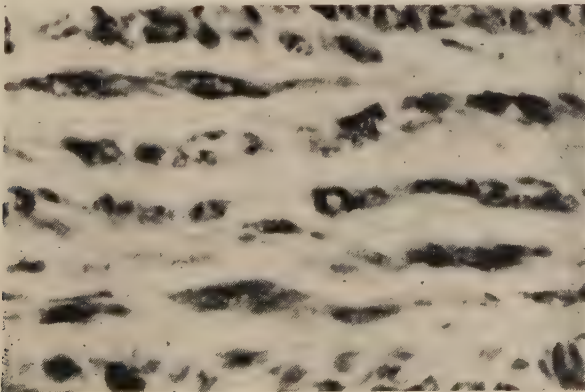


FIG. 1.—Aorta : Lipoids visible as aggregates of black granules in the muscle bundles. High power. Paraffin section : Sudan black.

Blood vessels: The arteries showed the most pronounced changes. Vascular changes were found in practically all organs examined, and were particularly marked in the kidney. Most striking was a broadening of the media, the smooth muscle fibres of which showed vacuolization. In polarized light, the muscle fibres of the media

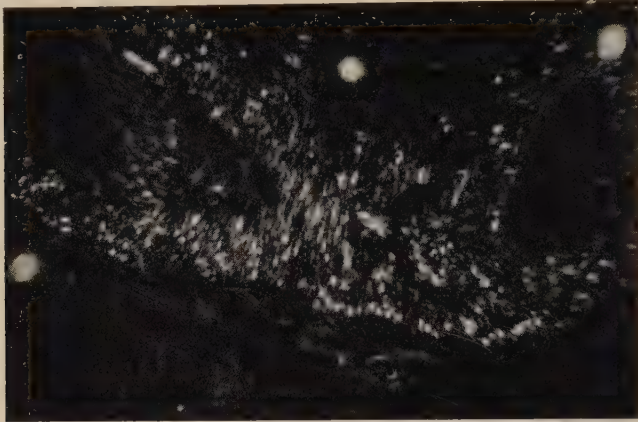


FIG. 2.—Middle-sized artery of the kidney: Vacuolated muscle cells of the media filled with doubly refractile substances. Polariscopic examination.

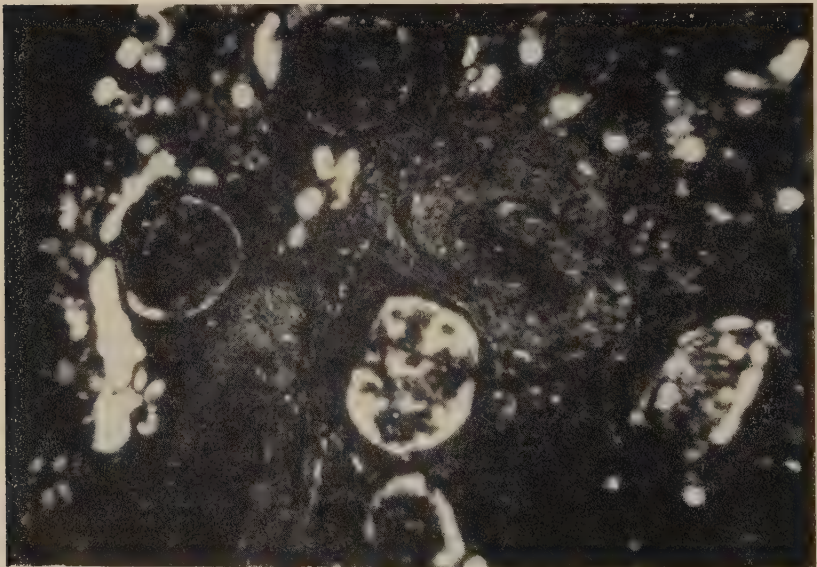


FIG. 3.—Kidney: Doubly refractile substances in arteries, in Bowman's capsules and Henle's loops. Polariscopic examination.

showed doubly refractile lipoids (Fig. 2). On staining with haematoxylin-scarlet red or Sudan black the vacuolised muscle fibres of the vascular coat proved to be filled with granular lipoids. Endothelial cells also proved occasionally to be stuffed with lipid granules.

Kidneys: Lipoids were demonstrable in the arteries as in the other organs. In addition, lipid deposition was found in the epithelium cells of Bowman's capsule and in those of Henle's loops (Fig. 3). In the latter the staining with scarlet-red was unusually clear: possibly this points to the presence of other fatty substances here besides the phosphatide which may be characteristic of angiokeratoma corporis diffusum.

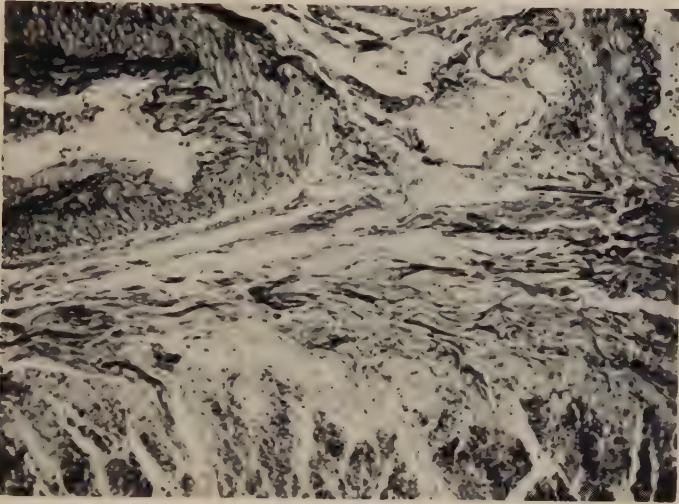


FIG. 4. —Ascending colon: Artery showing vacuolated muscle cells; structure of the smooth musculature of the intestinal wall locally blurred. H. & E.

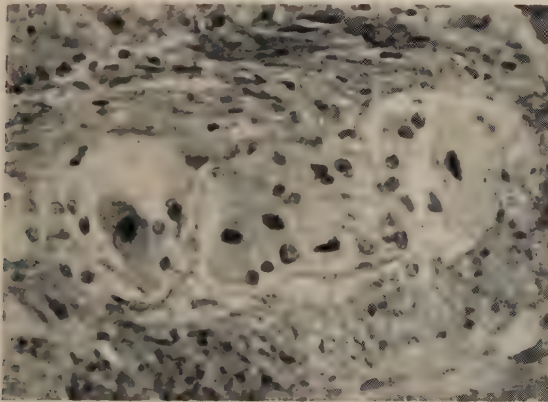


FIG. 5. —Ganglion cells of Auerbach's plexus: Markedly swollen cells showing a foamy structure with pycnotic nuclei pushed to one side. Nissle.

Ascending colon (H. & E.): Distinct vacuolisation of the smooth muscle fibres of the media of the arteries (Fig. 4): markedly swollen ganglion cells (Meissner's plexus, Auerbach's plexus), the cell body showing a foamy structure and the nuclei, for the greater part pycnotic, being shifted to the wall (Fig. 5). In places, the structure of the smooth musculature of the intestinal wall was blurred. Lipoid was found in the media of the arteries as in the other organs. The smooth muscle of the intestinal

wall showed doubly refractile substances in places. These could likewise be made visible by staining with haematoxylin-scarlet red. The contents of the pathologically changed ganglion cells proved to be doubly refractile (Fig. 6) and with haematoxylin and scarlet-red the cytoplasm of these ganglion cells appeared stuffed with small orange-red granules.



FIG. 6. Ganglion cells of Auerbach's plexus: The contents of the pathologically-changed ganglion cells are doubly refractile. Also doubly refractile substances in the smooth muscles of the intestinal wall. Polariscope examination.

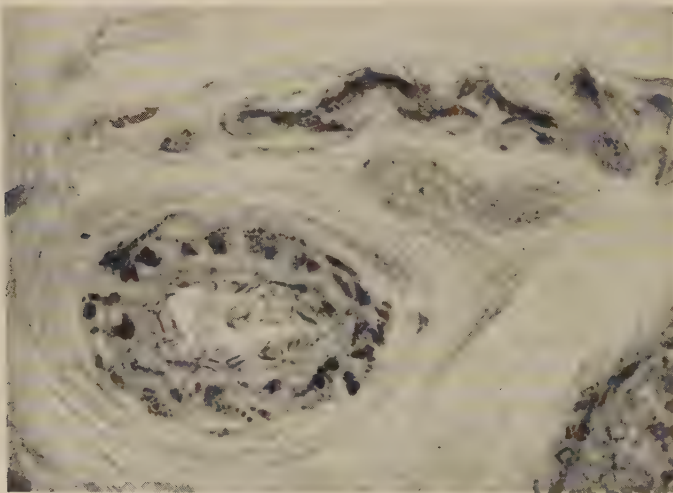


FIG. 7.—Skin: Arteriole with thickened wall due to broadening of the muscle layer. The media clearly contains lipoid. In the upper part a capillary cut lengthwise. The elongated endothelial cells are stuffed with lipoid granules, stained intensely black. Paraffin section: Sudan black.

Skin: Lipoids were demonstrable in practically all blood vessels, including the media of the arteries and arterioles, the smooth muscle of the adventitia of the veins and venules and the endothelial cells, notably those of the capillaries and the small veins (Fig. 7).

Owing to special circumstances, our examination was restricted to a limited number of organs. However the results so far obtained are quite in agreement with the findings of Scriba in the case of Hornbostel *et al.* (1951).

As to the nature of the lipid concerned in angiokeratoma corporis diffusum, chemical analysis of the cardiac muscle in Scriba's case showed a 10-fold increase of the diaminophosphatides. These differed from the sphingomyelins in solubility (Kühnau). In the present case extraction of the heart muscle resulted only in the isolation of an amorphous wax-like mixture. Later, however, Dr. Kühnau has isolated from the kidneys a definitely pathological lipid which shows great similarity to that found in Scriba's patient. Further research is being undertaken to determine the nature of this substance.

In conclusion, I would refer once more to the skin manifestations. The genesis of angiectases and vascular aneurysms which constitute the most conspicuous cutaneous changes in angiokeratoma corporis diffusum is largely dependent on alterations in the vascular wall and on haemodynamic factors. On histological examination it appeared that the walls in practically all categories of cutaneous vessels had been changed to a marked extent by the presence of lipoids. In addition to this, one can indicate various factors which would be expected to lead to irregularities in the pressure and blood flow in the cutaneous vessels. Vasomotor disturbances, possibly due to pathological alterations in the nervous system, are nearly always present in these patients and changes in vascular tone may be anticipated in view of the anatomical lesions. In the cases of Scriba and myself the factors summarised above could be largely ascribed to an underlying metabolic disorder, perhaps a lipoidosis. If these findings in angiokeratoma corporis diffusum can be adequately confirmed, a causal relationship between the cutaneous manifestations and the systemic condition should be established.

Precipitating factors also play a part in producing the skin lesions. Some years ago I saw a patient in whom fresh lesions had appeared at the place where a hot water bottle had been applied the day before. Angiokeratoma corporis diffusum is *not* a form of angiomatosis as has been assumed before now, but the changes (angiectases etc.), in my opinion, originate from pre-existent blood vessels. Histological examination in my cases did not reveal an increase in the number of blood vessels. In some patients ampulla-like dilatations of the small vessels of the fundus oculi have been observed. Histological examination of the intestine in the case under discussion revealed pronounced dilatation of the blood vessels and the formation of blood-filled cavities immediately under the mucosa. These findings were in every respect comparable with those met with in the skin. At the autopsy blue-red papules had been observed along the whole gastro-intestinal tract.

The skin affection is one of the principal features of the more complicated syndrome which angiokeratoma corporis diffusum is now recognized to be.

In contradistinction to the cutaneous changes the signs and symptoms of internal origin often occur late and, as a rule, are hardly pathognomonic. Accordingly, practically all the cases of this syndrome have been identified by the condition of the skin. It is true that cases have been described in which systemic manifestations have not been mentioned by the authors concerned, but it may be that the examination of the patients was incomplete in these cases.

In the course of studies performed so far, I have had the impression that lipoid is abundantly present particularly in the cutaneous vessels. It may therefore be possible to demonstrate the presence of the associated lipoid metabolic disturbance during the patient's life by means of skin biopsies. So far this has been done only in the second case of Hornbostel and Scriba (1953), namely by means of frozen sections in polarized light. Personally I had the opportunity a short time ago to examine a skin biopsy from a case recently diagnosed by Professor Prakken of Amsterdam. There I was able to demonstrate the presence of lipoid without difficulty, not only in polarized light but also by the staining techniques described in this paper. This observation contrasts with the findings of Fessas *et al.* and Pittelkow *et al.*, from which it appears that no doubly refractile or stainable lipoid substances could be demonstrated in biopsy specimens. This failure however may be explained by insufficiency of material for study and by the staining techniques applied in these cases. In my own experience, postchromation and staining with Sudan black appeared to be particularly useful for the demonstration of the lipoids where skin tissue was concerned.

REFERENCES.

- FESSAS, P., WINTROBE, M. M. and CARTWRIGHT, G. E. (1955) *Arch. intern. Med.*, **95**, 469.
 HORNBOSTEL, H., SPIER, W. and KOCH, H. (1951) *Arztl. Wschr.*, **6**, 49.
 ——— and SCRIBA, K. (1953) *Klin. Wschr.*, **31**, 68.
 KÜHNAU, J. Cited by K. Scriba (1951).
 PITTELKOW, R. B., KIERLAND, R. R. and MONTGOMERY, H. (1955) *Arch. Derm. Syph., Chicago*, **72**, 556.
 POMPEN, A. W. M., RUITER, M. and WIJERS, H. J. G. (1947) *Acta med. scand.*, **128**, 234.
 PRICE, J. H. (1955) *Brit. J. Derm.*, **67**, 105.
 RUITER, M. and POMPEN, A. W. M. (1939) *Arch. Derm. Syph., Wien*, **179**, 165.
 ——— (1946) *Ned. Tijdschr. Geneesk.*, **90**, 1757.
 ——— (1953) *Arch. Derm. Syph., Chicago*, **68**, 21.
 ——— (1954) *Dermatologica, Basel*, **109**, 273.
 ———, POMPEN, A. W. M. and WIJERS, H. J. G. (1947) *Ibid.*, **94**, 1.
 SCRIBA, K. (1951) *Verh. dtsh. path. Ges.*, **34**, 221.

JUXTA-ARTICULAR NODES.

AN ACCOUNT OF A CASE.

T. SALAMON.

Hospital for the Treatment of Mycotic Diseases, Banja Luka, Yugoslavia.

LUTZ (1891) and Jeanselme (1900) first reported on subcutaneous nodes or nodosities of solid consistence, painless and freely mobile, varying from the size of a pea to that of an egg, with a symmetrical localization in the region of the large joints, particularly on the extensor aspects of the elbows and knees. They termed this condition juxta-articular nodes (j.a.n.). Lutz's case originated from Honolulu and Jeanselme's from Indo-China. Later on, these cases were found also in Europe, in patients who had never left this continent (Hoffmann, 1932; Jessner, 1926).

These lesions have been attributed to framboesia or to syphilis, since certain authors, e.g. Van Dijke and Oudendal, have observed treponemata in them, and Jessner succeeded in transferring the syphilitic infection by inoculation of pathological products from man to animal. Further, the treponematous aetiology is confirmed by the fact that serological reactions to syphilis are positive in the majority of cases. In many text-books, therefore, j.a.n. are described as manifestations of framboesia or of syphilis.

If however j.a.n. are considered only from the morphological standpoint, and all clinically comparable lesions are grouped under this term, we have a clinical manifestation of the most varied aetiology and not only of treponematous origin. In this are included cases of primary chronic rheumatism, gouty diathesis, calcinosis of the skin, xanthomatosis, cystercosis and erythema elevatum diutinum, in which the clinical changes in the skin have the characters of j.a.n. Moreover, in 1954, Tagliavini described a case of j.a.n., having no relationship to any of the above mentioned groups of conditions. Hence, roughly morphologically, j.a.n. represents a fairly clearly defined clinical peculiarity of a varied aetiology.

The histological structure helps in some measure to separate certain conditions from the group. Thus for example xanthomata have a specific histological framework as have the nodules of calcinosis and of gout, whereas those which occur in treponematosis, in primary chronic rheumatism and in erythema elevatum diutinum have many common histological features. Hence the differential diagnosis between those latter conditions is sometimes very difficult.

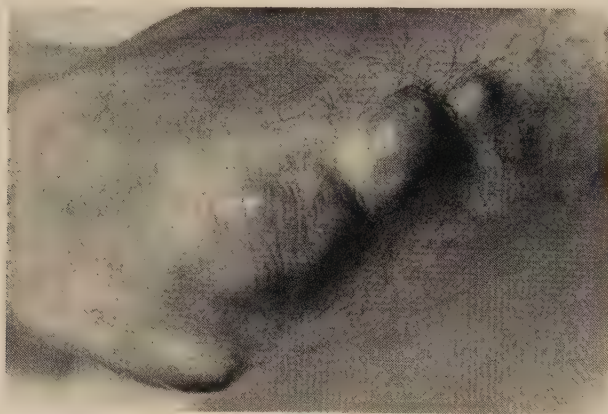
We ourselves have recently observed a case which merits the term j.a.n. Our case has not a treponematous aetiology, and indeed we have not been

able completely to elucidate the cause ; it belongs most likely to the rheumatic group.

CASE REPORT.

A countryman aged 52 consulted us on 11 June 1956 on account of a lesion near his anus. On examination of the skin we found a typical j.a.n.

Family history was negative. He did not remember any childhood diseases and according to his statement he had been healthy until 1943. In that year, nodules appeared on the extensor aspects of both elbows, during his captivity in Germany. They developed slowly, and were very hard. At the time he had considerable pains in the elbow joints, knees and sacral region. He had been treated with some injections, after which the pains were alleviated but the nodes had not disappeared. After his return from captivity in 1945, he noticed some lesions in the region of the anus, for which he had been treated without benefit. He complained of pains about the anus, particularly on walking. His appetite was good, his bowel habit regular. He denied venereal infection.



Present state.—In the region of the extensor aspect of the right elbow joint are four tumours of very solid consistence, all freely mobile. One tumour is the size of a cherry, and the others are considerably larger, up to the size of a nut (Fig. 1). The skin covering the tumours is livid, otherwise unaltered, and cannot be separated from the tumour. Over the extensor surface of the left elbow joint are five smaller tumours of rather hard consistence, the size of a maize grain, with a livid-coloured skin over their surface. These tumours are also freely mobile. On the extensor surface of the upper arm numerous brown pigmented lesions the size of a millet grain are present. Similar pigmentation, though not so dense, is seen on the skin of both buttocks, and on the flexor surface of the thigh is a *café au lait* macule 8 cm. $\times$ 4 cm., with tooth-like edges. In the region of the anus are three fistulae discharging pus on pressure.

The skiagram of both elbows shows no pathological changes in the joints and no calcification of the soft tissues.

Histology.—(Node of the right elbow). Hyperkeratotic epidermis, otherwise without particular changes, in places slightly atrophic. The fibrous hyaline tissue of the dermis is slightly infiltrated by lymphocytes. Chalky masses have not been found (Dr. M. Arambašić, Pathological Institute, Medical Faculty, University of Belgrade.)

Ophthalmological and E.N.T. examination—normal. The mucous membranes of the mouth, the tongue and the throat are normal. Lungs and heart clinically and radiologically normal. Abdominal organs, prostate, epididymis and testes—normal.

Blood count: Hb 75% otherwise normal. Urine normal.

Serological reactions to syphilis: Nelson and Meyer's test—negative. Mantoux 1:1000 $\pm$. Serum calcium 9.1 mg.%; Weltmann V, Gross negative, Cadmium negative, Hymans van den Bergh negative, bilirubin 0.3 mg.%, thymol 2. Serum cholesterol 135 mg.%. Serum proteins: albumin 55.1%; alpha glob. 11.7%; beta-glob. 14%; gamma glob. 19.2%. Löwenstein culture of pus discharging from the fistule in the region of the anus: positive.

Treatment.—Because of the tuberculous anal fistulae he was given calciferol therapy (weekly one ampule of 600,000 units by mouth), followed by Eutison,* 500 mg. daily. Thereafter the patient was submitted to surgical intervention.

It is interesting to point out that after six weeks' therapy with calciferol and Eutison the nodes appeared to be smaller and softer than before and were no longer attached to the skin.

DISCUSSION.

First of all, we may establish with certainty that the nodes have no relationship to syphilis, since the classical serological reactions to syphilis and the Nelson-Meyer test are negative. Neither are they an abortive form of Recklinghausen's disease.

From an aetiological point of view, there remain two possibilities: either the nodes are aetiological in connection with primary chronic rheumatism, which the case history indicates; or there exists a causal relationship between the tuberculous fistulae and the nodes, this latter thesis being more probable.

Several authors have affirmed that there are cases of j.a.n. in which Koch's bacillus is the aetiological agent. Since our patient had fistulous changes of the anus, of tuberculous nature, and since we observed some changes in the nodes during treatment with calciferol and Eutison, it is probable that Koch's bacillus is the determinant of the j.a.n. in our case.

SUMMARY.

Description of typical juxta-articular nodes in a 52-year-old man, suffering from a tuberculous anal fistula. The serological reactions to syphilis and Nelson-Meyer's test were negative. In the history of the patient there were rheumatic pains in the joints at the time of the appearance of the nodes. Calciferol and Eutison therapy had a certain effect on the nodosities.

REFERENCES.

- DIJKE, VAN and OUDENDAL. Quoted by Darier, J., Civatte, A. and Tzanck, A. (1947) *Précis de Dermatologie*. 5^e édition, p. 391. Paris: Masson et Cie.
 HOFFMAN, H. (1932) In *Jadassohn's Handbuch der Haut- und Geschlechtskrankheiten*. Band XII/I, p. 419. Berlin: Julius Springer.
 JEANSELME (1900) quoted by Hoffmann.
 JESSNER, M. (1926) *Arch. Derm. Syph., Wien*, **152**, 132.
 LUTZ, A. (1891) quoted by Hoffmann.
 TAGLIAVINI, R. (1954) *Arch. ital. Derm.*, **26**, 383.

* Eutison is Isonicotinic acid hydrazide.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. LOUIS FORMAN.

19 April 1956.

Benign Lymphocytic Infiltration of the Skin.—Dr. D. L. REES (for Dr. G. B. DOWLING).

G. W.—, male, aged 49 years.

History.—Rash on the face for 18 weeks and pain in the chest for 16 weeks.

The first symptom was the development of red patches on the face and angles of the jaw. These were irritable and have persisted.

Two weeks later he developed retrosternal pain and vomited. There were two similar attacks within the next week or two, associated with pain in the left side of the head and left ear. Later he complained of a cough.

Examination.

Enlargement of lymph glands of the left cervical chain and sub-occipital regions.

Chest.—Dull to percussion over the left sub-clavicular region.

Skin.—There is an eruption of slightly raised erythematous patches on the face, forehead and angles of the jaw.

Investigations.

W.R.: Negative.

W.B.C.: 6500 with normal differential count.

B.S.R.: 6 mm. in 1 hour.

Chest x-ray: Large opacity in the left upper hilar region.

Biopsies.—(a) Cervical gland: Anaplastic carcinoma. (b) Skin: Normal epidermis with focal infiltration of mature lymphocytes in the dermis. No neoplastic cells.

Comment.

This condition was first described by Jessner in America in 1953 who followed a group of cases for ten years and described their clinical characteristics as follows:—

There are erythematous lesions varying from papules to macules, sometimes assuming a circinate form, nearly always on the face, which are subject to spontaneous remissions and recurrences over a long period. The histology shows fairly regular lymphocytic infiltration in the mid-dermis. There are no changes in the epidermis or any alteration of the collagen. About differential diagnosis, he remarks that the condition is probably fairly common and the conditions most usually mistaken for it are the unstable form of lupus erythematosus, erythema annulare and the erythematous variety of sarcoid.

This case has another interesting feature because the skin lesions developed on the face four months ago and a fortnight later he developed symptoms that on investigation were found to be due to an anaplastic carcinoma of the lung.

It is conceivable that there may be some connection between the carcinoma and the

skin lesions; the latter possibly being caused by malignant emboli from the lung tumour. It can be difficult histologically in such circumstances to pick out the malignant cells. The other possibility is that this is a toxic eruption connected with the neoplasm, analagous to dermatomyositis when accompanied by a malignant neoplasm.

REFERENCE.

JESSNER, M. (1953) *Arch. Derm. Syph., Chicago*, **68**, 447.

Reticulum-cell Sarcoma of the Skin.—Dr. D. L. REES (for Dr. H. J. WALLACE).

F. P.—, male, aged 42 years.

History.—Red patch under the left nipple noticed 15 years ago. Multiple small pink nodules each about 0.5 cm. in diameter appeared in the same area about 10 years later when he first came for treatment.

The large areas of atrophic scleroderma on his back have been present as long as he can remember, and they have not altered within his recollection since childhood.

Examination.

Several small pinkish-yellow slightly infiltrated lesions in the xiphisternal area and in the pubic area.

Large atrophic telangiectatic sheets in the lumbo-sacral area.

No enlargement of superficial lymph glands.

Chest.—N.A.D.

Abdomen.—Liver and spleen, normal.

Investigations.

Chest skiagram : N.A.D.

Two differential white cell counts (January 1951 and April 1956) : Normal.

Biopsies (Dr. Whimster).

October 1950.—Heavy dermal infiltration with cells of various types. Could be part of a leukaemia of a reticulosis.

April 1952.—Reticulum-cell sarcoma.

April 1956.—Reticulum-cell sarcoma.

Progress and Treatment.

The original lesions responded rapidly to a total dosage of 1000 r each at 70 kV.

October 1950 to December 1953.—Fresh groups of nodules developed near both nipples, on the pubes, and in the dorso-lumbar region of the back at various times. They all responded quickly to radiotherapy in the above dosage, and did not recur.

December 1953 to September 1955.—No fresh lesions.

September 1955 to April 1956.—Gradual development of lesions now present.

Comment.

The point I wish to make is on the prognosis of this particular variety of reticulosis. This man has had the condition for 15 years without any signs of distant metastases and I have observed three other patients with a similar histology, two of whom have been affected for over 5 years with a small number of lesions on the trunk. The third died after 15 years with generalized metastases.

There is an interesting section by Lumb (1954) in his book in which he described 20 cases with this histology occurring in lymphatic nodes and bone where they are much more common than in the skin. He gives a very low 5 years' survival rate. Apparently they die of distant metastases. If they develop leukaemia it is of the monocytic type.

The apparent difference in prognosis between the skin cases and the deep cases can be explained by the fact that the skin cases are diagnosed far earlier. In the lymphatic node cases there may be latent periods before symptoms result in diagnosis.

REFERENCE.

LUMB, G. D. (1954) *Tumours of the Lymphoid Tissue*, Edinburgh: E. & S Livingstone.

Candida Infection of the Nail Plate Resembling Trichophyton Infection.— Dr. BRIAN RUSSELL.

History.—Miss L. L., aged 50, began to develop mild Raynaud's phenomenon at the age of 14. Since the age of 20 this has been severe and accompanied by perniosis affecting both hands but not the feet. For 20 years the nails have been affected. At first there was paronychia; the nails of the thumbs and all the fingers have been affected at one time or another except the nail of the left little finger. For the last 3 years there has been no paronychia, but the left middle finger nail has remained distally detached from its bed.

Past treatment.—Several nails have been removed but the condition has recurred. The nail fold of her left index finger was treated by curettage on one occasion with resulting pterygium.

Condition on examination.—Pterygium and dystrophy of the nail of the left index finger. Longitudinal ridging of the middle finger nail, with greyish-brown discoloration of the distal half which is detached from its bed. Toe nails normal.

Urine: No abnormality found.

Mycological reports.—Right thumb nail and left middle finger nail: fungus present. In some places it suggests monilia but in others it is indistinguishable from true ringworm fungus.

Culture from the nail plates on four occasions in New Zealand and on four occasions at St. John's Hospital has grown *Candida albicans*. No dermatophyte has ever been isolated. No fungus or monilia has been found in finger webs, palm, toe nails, toe webs, or the heel, and no dermatophyte has been grown from any of these sites.

Treatment.—There has been no response to treatment with thorium-X 1500 e.s.u. on four occasions; to zinc undecylenate ointment; to ammoniated silver nitrate; or to Mycostatin.

Comments.

It is often difficult to culture fungi recovered from nail plates and it is possible that some of the mycelial filaments were those of a pathogenic dermatophyte, but there is no evidence of trichophytosis elsewhere and the history of Raynaud's phenomenon and of paronychia supports the diagnosis of candidiasis of the nails.

DISCUSSION.

The PRESIDENT: Raynaud's disease, if severe, may lead to dystrophy of the nails, and then *Candida* may invade them.

Dr. B. RUSSELL: I think the *Candida* has invaded nail plates that were already abnormal.

Dr. C. D. CALNAN: It is always difficult to decide whether the *Candida* is a primary pathogen, or merely secondary to a dystrophy of the nail in these cases. But *Candida* was grown repeatedly and consistently in pure culture, both in this patient and in a few others whom I have seen.

A similar condition of moniliasis of the nails in the absence of chronic paronychia, is found in about 10% of patients with idiopathic hypoparathyroidism.

I believe Dr. Wigley has recently had a patient with moniliasis of the nails, similar to Dr. Russell's. A nail biopsy should be done and might reveal true invasion of the nail tissue.

Urticaria Pigmentosa.—Dr. R. H. MARTEN (for Dr. SYDNEY THOMSON).

L. H.—, aged 9 years.

History.—Brown spots were first noticed in the region of the left shoulder when he was about 18 months old. Since then other patches have gradually appeared on the chest and abdomen. During the past 4 years he has developed irritating bumps and brown areas in his scalp. From time to time blisters and weeping areas have occurred on the scalp, but never on the chest or back.

No new lesions have appeared in recent months and existing lesions are perhaps slightly paler. Over the past 4 years he has also suffered from attacks characterized by sudden flushing of his face, arms and legs, listlessness and shivering unaccompanied by rise in temperature. In these attacks, which may occur at any time and last about 25 minutes, he has never lost consciousness. There have been long intervals between these episodes which have been less frequent since tonsillectomy in June 1955. Otherwise his general health is satisfactory.

Family History.—No skin trouble.

Examination.—Over the trunk, back and abdomen is an eruption of brown macules of differing sizes and shapes which urticate on gentle rubbing. In addition, at various times he has shown considerable dermographism. The limbs and face are not affected apart from a single pink lesion in the region of the right eyebrow. Scattered over the scalp are a large number of round or oval macules varying in colour from yellow-brown to pink. There is no atrophy or definite loss of hair over these areas. Apart from the liver edge which can be felt on inspiration there are no other abnormalities.

Investigations.

Blood count.—Haemoglobin 82%, white cell count 8400/c.mm. Normal film.

E.S.R.—2 mm./hour (Wintrobe).

Bleeding time.—3 minutes.

Clotting time.—6½ minutes (Lee and White's method).

Prothrombin time.—14 seconds.

Prothrombin concentration.—90%.

Skiagram of skeleton.—No bony abnormality.

Histology (biopsy from pink area on scalp).—A cellular fairly well circumscribed mass occupies almost the whole thickness of the corium and is composed of large numbers of oval and spindle-shaped cells together with occasional eosinophils and lymphocytes. Special staining shows all the oval and spindle cells to be mast cells. There is some increased pigmentation in the basal layer of the epidermis.

Treatment.—Chloroquin 200 mg. daily for one month without improvement.

1% Efcortelan lotion daily to one area on the scalp without benefit.

Comment.

There are several points of interest. First, the heavy involvement of the scalp is unusual. Furthermore, in the absence of lesions elsewhere the appearance of the scalp lesions especially the pinker ones might lead to some diagnostic difficulties.

It seems likely that the attacks of severe flushing of the limbs and face are also related to his urticaria pigmentosa, as on a number of occasions they have been associated with much elevation and irritation of the scalp lesions. It may be that these attacks are mediated through the liberation of histamine, although reproduction of these attacks by means of histamine injection has not been attempted. Although recent papers have stressed the possibility of urticaria pigmentosa being a manifestation of systemic disease, we have been unable to demonstrate any convincing evidence of systemic involvement in this patient.

DISCUSSION.

The PRESIDENT : This interesting case is the first one shown with constitutional symptoms.

Dr. R. E. BOWERS : I have seen one similar patient, an infant, who became drowsy and whose skin flushed deeply whenever any of the lesions was rubbed firmly.

Dr. R. H. MARTEN : A visit to the barber always brings on one of these attacks.

The following cases also were shown :

Pyoderma Gangrenosum.—Dr. L. FORMAN and Dr. AITKEN ROSS.

Pyoderma Vegetans.—Dr. D. L. REES (for Dr. H. T. WALLACE).

Lymphoid Follicular Reticulosis.—Dr. J. S. PEGUM.

Juvenile Melanomata.—Dr. J. MORGAN.

Atrophic Lichen Planus.—Dr. R. G. HOWELL (for Dr. G. B. MITCHELL-HEGGS).

Extensive Perniosis.—Dr. G. A. BECK.

CORRESPONDENCE.

The Editor, 'The British Journal of Dermatology'.

SIR,—The interesting article by Drs. E. A. Fairburn and W. Frain-Bell on "Rat-mite dermatitis", prompts me to recall a similar outbreak in a paper factory which I have described in the *Veterinary Record* (1955, **67**, 883). The few workers affected complained of intense itching of the limbs, where only scratch marks were to be seen. Their work was shovelling pulverized esparto grass in a yard which was infested with brown rats. The grass had been imported from Eritrea, and in it Dr. Richard Mawson of King's Langley found some mites, which were identified as *Hypoaspis fenilis* (Méglin, 1875) by Dr. E. Browning of the British Museum of Natural History. This mite is less common than *B. bacoti*, and seems to be capable of surviving for a considerable time on vegetable fibres without an animal or human host. The only other recorded outbreak I know of due to this mite was among American troops in North Wales during the war. The source of infection was traced to the straw in their newly-filled palliasses (Hill, M. A. and Gordon, R. M. (1945) *Ann. trop. Med. Parasit.*, **39**, 46).

In most recorded outbreaks of rat-mite dermatitis the buildings contain paper-pulp or straw. This may be because rats select such materials for nesting; or perhaps, as in the case of other mites and *H. fenilis*, because these vegetable fibres provide an adequate diet.

Yours sincerely,
IAN MARTIN-SCOTT.

London,
December 1956.

CURRENT LITERATURE

LUPUS ERYTHEMATOSUS AND HYDRALAZINE. R. L. TOURAINE. (1956) *Ann. Derm. Syph.*, **83**, 158.

An L.E.-like syndrome occurs in possibly 10% of patients treated with hydralazine for hypertension. After vague premonitory symptoms the patient develops joint pains, fever, transient skin rashes especially on the face and hands, enlarged glands and spleen and other signs. The most striking laboratory finding is the presence of typical L.E. cells in the blood. The syndrome disappears rapidly on stopping the drug. Giving hydralazine to dogs produced similar changes. The author discusses various hypotheses which might explain these observations.

F. F. H.

FUNCTIONAL EXPLORATION OF THE SKIN. S. JABLONSKA. (1956) *Ann. Derm. Syph.*, **83**, 247.

The author lists the various methods of exploring the function of the skin used in Warsaw. These include measurement of chronaxie in the sensory nerves, the changes of temperature in one hand when the other is warmed or cooled, reheating curves after cooling the skin, capillaroscopy, etc. He believes these are of great value in diagnosis as for instance in distinguishing scleroderma from Raynaud's disease and in following the response to treatment which is illustrated by the action of Vitamin E on scleroderma.

F. F. H.

CUTANEOUS LEISHMANIASIS IN VENEZUELA. JORGE HOMEZ. (1956) *Ann. Derm. Syph.*, **83**, 271.

The author reviews the history, clinical symptoms and diagnosis and describes 7 cases. Five of these were cured with glucontime, an organic antimony compound, and 2 by the anti-malarial drugs, Aralin and Nivaquin.

F. F. H.

SYSTEMIZED AMYLOIDOSIS. R. DEGOS. (1956) *Ann. Derm. Syph.*, **83**, 361.

This is an excellent summary of the present state of knowledge about this rare condition together with two striking pictures of macroglossia. Systematized amyloidosis has been associated with multiple myeloma in 20 of 105 reported cases of the former. The relationship between the two is not yet clear though both may show a great increase of serum globulin, especially the α -fraction. It is possible that disequilibrium of the serum globulin may play an important part in the development of the amyloidosis.

F. F. H.

SUBACUTE MIGRATING NODULAR "HYPODERMITE". X. VILANOVA and J. PINOL AGUADÉ. (1956) *Ann. Derm. Syph.*, **83**, 369.

Gougerot described 12 types of "hypodermite". The 11 cases here presented approximate to his second group "hypodermite en plaques indurées" but are sufficiently distinct to justify separation. All the patients were women from 22 to 54 years old and 8 had recently had an attack of tonsillitis. From 1 to 20 days after, a pea-sized subcutaneous nodule appeared, usually on the antero-lateral aspect of the leg. The nodule was not painful and not adherent to the skin and deeper structures; slowly it would extend until it measured 10 to 12 cm. There was never any bruised appearance. After a period varying from a week to 3 months the lesion resolved, the only effective treatment being potassium iodide. Histologically the primary lesion was a capillaritis in the hypoderm. The authors distinguish the condition from erythema nodosum, Parkes Weber disease and other conditions. A very full bibliography is given.

F. F. H.

LEUCODERMA. B. N. BANERJEE and S. K. PAL. (1956) *Ind. J. Derm.*, **1**, 1.

Meladinine is an effective treatment for the majority of patients and probably works as well when simply painted on the patches as a tincture, as when also given by mouth. The tincture is often better diluted, should be applied twice daily. Exposure to the sun is not desirable. The authors feel that intestinal parasites play a part in the aetiology of vitiligo, give details of

125 cases 85% of which were infested, and suggest better results of therapy when this infestation is abolished and vitamin B complex and additional protein are added to the diet.

R. D. S.

THE SUBJECT OF DERMATOLOGY.—Editorial, *Ind. J. Derm.*, 1, 83.

"It is inconceivable why for years gone by the subject of Dermatology was linked together with that of Venereology or Syphilology . . . nay gonorrhoea . . . is by no stretch of the imagination a skin disease. It will be ridiculous to think of a dermatologist treating a case of gonorrhoea and giving urethral irrigation . . . Besides, Dermatologists and Venereologists are looked upon from different social standpoints . . . The public do not like exposure, they prefer attending a venereological clinic at night . . . Dermatology must not be linked with Venereology . . . From the British Journal of Dermatology and Syphilology, Syphilology has been excluded . . .

"We have an Indian Journal of Dermatology and Venereology published in Bombay . . . We have started in Calcutta an Indian Journal of Dermatology . . . We dermatologists of India should have a journal of Dermatology alone and we have got it at last."

R. D. S.

VALUE OF ISONICOTINIC ACID HYDRAZIDE (I.N.H.) IN THE TREATMENT OF LEPROSY (A REVIEW). S. GHOSH and N. MAKERJEE. (1956) *Ind. J. Derm.*, 1, 85.

I.N.H. alone has a definite effect in the first two or three months, especially in reducing bacteriological concentration, but the initial improvement is not maintained. Combined therapy with D.D.S. is of value, probably mainly by delaying the development of drug resistance.

R. D. S.

REVIEW OF ADENOMA SEBACEUM WITH CASE NOTES. B. N. BANERJEE and R. PANJA. (1956) *Ind. J. Derm.*, 1, 98.

An excellent description of the whole syndrome: 7 cases are described, 5 with a family history: 2 were epileptic. One patient had a child with tuberous sclerosis. Another with the Pringle type had an associated naevus anaemicus and a mother with multiple benign cystic epitheliomata.

R. D. S.

CHRONIC BENIGN PEMPHIGUS OF HAILEY AND HAILEY. R. V. RAJAM, P. N. RANGIAK, A. S. THAMBAIAH and V. C. ANGULI. (1956) *Ind. J. Derm. Vener.*, 22, 73.

An interesting case is presented, a middle-aged woman with 12 years' history of recurrent attacks confined to the axillae groins and flexor aspects of the elbows, knees and thighs. These areas cleared completely between attacks which occurred particularly in hot, humid weather. The histology was typical, with fairly superficial acantholysis; there was no dyskeratosis. The authors, after reviewing bullous eruptions very completely, consider Hailey and Hailey's disease is not related to Darier's disease.

R. D. S.

A SIMPLE METHOD FOR PREPARING POWDERED SKIN. F. FLESCH. (1955) *J. invest. Derm.*, 25, 209.

"Whole skin or corium is cut into pieces not exceeding about 4 square inches. The subcutaneous fat is removed and the species (sic) are dried by one of the standard methods at any desired temperature or *in vacuo*. Hard keratinous structures are broken or cut into small pieces. The dried pieces are then broken up in a Waring blender in the dry state without homogenizing liquid. The fragments then are passed through a Wiley mill . . ." (One would have supposed that the choice of methods for desiccating such large pieces of skin without too much chemical change would be more limited.)

J. H. T. D.

TIME FACTORS OF ERYTHEMA AND PIGMENTATION PRODUCED BY ULTRAVIOLET RAYS OF DIFFERENT WAVELENGTHS. A. BACHEM. (1955) *J. invest. Derm.*, 25, 215.

The 3 main bands for erythema and pigmentation are at 254, 297, and 365 m μ . The first is obtained from a low pressure high voltage cold quartz lamp by filtration through "bromine-chlorine vapour"; the second through CuSO₄ from a Kromayer lamp and the third through Corning No. 5874 from a medium pressure high voltage mercury arc.

The long wave reaction has no latent period and the duration of its erythema varies between 10 minutes and 24 hours, the pigmentation lasting anything up to a year or so. The medium and short waves have latent periods of 3 hours for erythema lasting about 4 days, and 24 hours for pigmentation lasting about a month, respectively.

J. H. T. D.

THE ADRENERGIC INNERVATION OF THE APOKRINE (CERUMINOUS) GLAND OF THE HUMAN EAR CANAL. E. T. PERRY, H. J. HURLEY, M. B. GRAY and W. B. SHELLEY. (1955) *J. invest. Derm.*, 25, 219.

Bielchowsky's silver impregnation method, modified for use with paraffin sections, displays the nerve fibres. Staining for specific and nonspecific cholesterinase activity indicates that they are not cholinergic. It is therefore presumed that they are adrenergic motor fibres of the autonomic nervous system. J. H. T. D.

STUDIES OF THORIUM X APPLIED TO HUMAN SKIN. IV. CLINICAL AND AUTORADIOGRAPHIC FINDINGS FOLLOWING THE INTRODUCTION BY IONTOPHORESIS. PAUL FLEISCHMAJER and V. H. WITTEN. (1955) *J. invest. Derm.*, 25, 223.

A much more intense reaction is obtainable by the use of 0.3 ma per sq. cm. for 20 min. (The difficulty of obtaining an even penetration over larger areas remains.) J. H. T. D.

CLINICAL INVESTIGATION IN DERMATOLOGY. C. S. LIVINGOOD. (1955) *J. invest. Derm.*, 25, 203.

Contains a few references to papers relevant to the subject.

J. H. T. D.

STUDIES ON URTICARIA PIGMENTOSA: I. RELEASE OF A HEPARINOID MATERIAL INTO THE CIRCULATION FOLLOWING DIRECT STIMULATION OF URTICARIA PIGMENTOSA LESION. F. URBACH, W. N. BELL and C. JACOBSON. (1955). *J. invest. Derm.* 25, 211.

The heparin released, though measurable by gamma protamine titration, was not enough to affect the clotting time. Nor was the oil clot retraction time or prothrombin consumption altered quite as much as they would have been with comparable doses of commercial heparin.

J. H. T. D.

THE EFFECT OF CORTISONE IN ALOPECIA AREATA. H. R. RONY and D. M. COHEN. (1955) *J. invest. Derm.*, 25, 285.

The practical value of all this is summed up in the legend to the illustration "Hair growing in a case of alopecia universalis in area injected intradermally with hydrocortisone. Photographed tangentially against a black background. Magnified $8\times$. Difference in length and thickness of hair is partly due to varying distance of the hairs from the camera".

J. H. T. D.

PERCUTANEOUS ABSORPTION OF HYDROCORTISONE-4-C¹⁴ IN TWO HUMAN SUBJECTS. F. D. MALKINSON and E. H. FERGUSON. (1955) *J. invest. Derm.*, 25, 281.

By means of C¹⁴-tagged hydrocortisone it is shown that absorption may occur through inunction of the healthy flexor surface of the forearm. But less than 1% of the hormone used was excreted in the urine as tetrahydro-hydrocortisone during the subsequent 6 days and most of that during the second 24 hours. Both its initial appearance in the urine and its final clearance were subject to delays which the authors interpret as the effect of local retention.

J. H. T. D.

HISTOLOGIC OBSERVATION ON THE HUMAN APOKRINE SWEAT GLAND IN HEALTH AND DISEASE. W. B. SHELLEY and E. J. LEVY. (1955) *J. invest. Derm.*, 25, 249.

A most valuable addition to the iconography of the apocrine gland. But the attempt to establish particular specific apocrine diseases—for example to make an "apocrine miliaria" of the Fox Fordyce syndrome—is not altogether successful.

A remarkable reaction of the gland to banal inflammation, most convincingly portrayed in the microphotographs, the authors call squamous metaplasia.

J. H. T. D.

CULTIVATION STUDIES ON WART SUSPENSIONS OF VERRUCA VULGARIS AND CONDYLOMA ACUMINATUM. B. V. SIEGEL and F. G. NORY. (1955) *J. invest. Derm.*, 25, 265.

A suspension in saline of warts ground in a mortar with sand is all that is meant by the words of the title. The work represents a failure to confirm the results of Bivins (*J. invest. Derm.*, 20, 471) either on chorioallantoic membrane or on tissue cultures of monkey kidney or human carcinoma cervicis. Nor did the authors succeed in demonstrating the virus by means of the ultramicroscope; but the warts were selected at random without any attempt at histological differentiation.

J. H. T. D.